UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,355	07/05/2006	Karin Butz	085449-0180	6994

22428 7590 04/18/2007
FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
SHIN, DANA H	
ART UNIT	**PAPER NUMBER**
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,355	BUTZ ET AL.	
	Examiner	Art Unit	
	Dana Shin	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-27 and 39-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-27 and 39-43* is/are rejected.

7)☒ Claim(s) *20,24 and 43* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

This Office action is in response to the communications filed on March 12, 2007.

Currently, claims 20-27 and 39-43 are pending. Applicants have cancelled claims 1-19 and 28-38.

The following rejections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Objections/Rejections

Claim Objections

Claims 20, 24, and 43 remain objected to for containing non-elected subject matter. Appropriate correction is required.

Applicant's arguments filed on March 12, 2007 have been fully considered but they are not persuasive. Applicant continues to traverse the restriction requirement among SEQ ID NOs. Note that the restriction requirement was made FINAL in the previous Office action for the

reasons stated in the Office action mailed on November 27, 2006 and for the reasons stated below.

As stated previously, applicant's traversal was on the ground that there is no serious burden on the examiner to search all 8 distinct SEQ ID NOs. Applicant was informed in the previous Office action that the issue of "search burden" was neither stated nor asserted in the Office action because the present application was filed under 35 U.S.C. 371 and 37 CFR 1.495. See page 3. Furthermore, each SEQ ID NO claimed in the instant case is not regarded as species but as separate inventions as expressly stated in the original Election/Restriction Office action mailed on September 29, 2006.

Since the restriction requirement was still deemed proper and made FINAL in the previous Office action on the merits, the pending claims will be examined on the merits only insofar as SEQ ID NO:2.

Claim Rejections - 35 USC § 112

Claims 20-27 and 39-43 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for the reasons stated in the Office action mailed on November 27, 2006 and for the reasons stated below.

Applicant's arguments filed on March 12, 2007 have been fully considered but they are not persuasive for the following reasons:

First, applicant argues that the specification discloses experiments performed *in vitro* with SEQ ID NO:4, which is within the genus of sequences comprising SEQ ID NO:2. Applicant is correct that SEQ ID NO:4 comprises SEQ ID NO:2 and its complementary sequence;

however, the instant disclosure provides only *in vitro* examples as expressly acknowledged by applicant, from which an *in vivo* method for decreasing expression of livin comprising SEQ ID NO:2 or a medicament for treatment of therapy-resistant tumors comprising SEQ ID NO:2 cannot be extrapolated, and would therefore require undue experimentation of one of ordinary skill in the art to make and use the entire scope of the claimed invention at the time of filing. Further, *in vivo* application of siRNA molecules for therapeutic purpose was neither predictable nor routine in the art as of the earliest priority date sought in the instant case. See pages 7-10 of the previous Office action mailed on November 27, 2006.

Second, applicant argues that a rigorous or an invariable exact *in vitro/in vivo* correlation is not required.

Applicant cites *Cross v. Iizuka,* 224 USPQ 739 (Fed. Cir. 1985), in which the Board found that the "knowledge as to the use of the pharmacological activity disclosed in the Japanese priority application lay in the fact that the system was a microsome system, ***microsome systems admittedly being known to those skilled in the art.*** Employing a microsome assay, the skilled worker could determine the relative strength of the compounds of the count vis-a-vis the known parent imidazole and 1-methylimidazole compounds. Thus, ***the dosage in the microsome assay milieu could be determined without inventive skill or undue experimentation***." The Board found that there was ***sufficient credible evidence*** that one skilled in the art, without the exercise of inventive skill or undue experimentation, could determine the dosage level, and therefore, the Board held that the disclosure of the Japanese priority application adequate to satisfy the first paragraph of §112. In sum, the court affirmed the Board's decision that rigorous correlation of

pharmacological activity between disclosed *in vitro* utility and *in vivo* activity is not necessary ***where disclosure of pharmacological activity is reasonable based upon probative evidence.***

In the instant case, the specification does not provide any probative evidence based on which *in vitro-in vivo* correlation can be reasonably made. Unlike the imidazole-derivatized compounds of *Cross v. Iizuka,* the siRNA molecules of the instant case and their *in vivo* pharmacological activity were unknown to those skilled in the art and therefore the dosage or pharmacological efficacy of the siRNA molecules would have required undue experimentation, especially since there is no sufficient credible evidence or reasonable probative evidence showing one of ordinary skill in the art can make a direct *in vitro-in vivo* correlation solely based on the content of the instant disclosure and the direction/guidance provided by the applicant.

Third, applicant argues that *in vitro* data may be sufficient to enable claims to *in vivo* embodiments.

Applicant cites a Federal Circuit decision made in *In re Brana*, 34 USPQ2d 1436 (Fed. Cir. 1995), which noted that "test results showing that ***several compounds*** within the scope of the claims exhibited ***significant antitumor activity*** against the L1210 ***standard tumor model in vivo.*** Such evidence alone should have been sufficient to satisfy applicants' burden."

Contrary to the several compounds tested *in vivo* in *In re Brena,* the instant specification discloses only a single compound (SEQ ID NO:4 embracing instantly elected SEQ ID NO:2) within a partial scope of the claims was disclosed, and moreover, no *in vivo* example was disclosed in the specification. Applicant's argument citing *In re Brana* is therefore non-analogous and irrelevant to the instant case, because several compounds showing significant

antitumor activity in a standard tumor model *in vivo* was considered to satisfy the enablement requirement in *In re Brena.*

Finally, applicant argues that even if some *in vivo* embodiments would be inoperative, this would not be determinative.

Applicant cites *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.,* in which the district court credited testimony by Atlas' expert, to the effect that he had successfully formed a number of detonable emulsions using a variety of emulsifiers specified in the Atlas' patent. Further, the district court found that ***one skilled in the art would know which emulsifiers would work in a given system, and therefore the amount of experimentation would not be unduly extensive.*** Further, the claim at issue was directed to an emulsion blasting agent and thus one skilled in the art would know how to select a salt and fuel and then apply "Bancroft's Rule" to determine the proper emulsifier, which the district court found to be a "basic principle of emulsion chemistry".

Since the instantly claimed subject matter bears no physical, chemical, or biological similarities with the emulsifiers claimed in the *Atlas* case, there is no nexus between the applicant's cited court decision and the enablement issues with respect to *in vivo* pharmaceutical activity of siRNA molecules. Further, unlike the *Atlas* case, which enabled one skilled in the art to determine the proper emulsifier based on a basic principle of emulsion chemistry, the siRNA technology performed *in vivo* was far from being basic or well-established as of the priority date sought in the instant case. See pages 7-10 of the previous Office action with respect to the unpredictability of siRNA activity *in vivo.* Again, the court decision cited by applicant is irrelevant to the enablement issue in the instant case.

New Rejections Necessitated by Amendments

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21 and 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claims are amended to recite "said nucleic acid has a length of 19-21 nucleotides". Although the length of instantly elected SEQ ID NO:2 is 19 nucleotides, there is no disclosure in the specification that teaches the instantly recited length limitation of "19-21 nucleotides". Accordingly, the amendments entered in the claims introduce new matter, which is unsupported by the specification.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 23 and 27 recite the limitation "said administration" in line 1. There is insufficient antecedent basis for this limitation in the claims because the term "administration" is not recited in claims 20, 24, or 26.

Conclusion

No claim is allowed.

This application contains SEQ ID NOs:1 and 3-9, drawn to inventions nonelected without traverse in the reply filed on June 26, 2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

J. DOUGLAS SCHULTZ, PH.D.
SUPERVISORY PATENT EXAMINER